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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/990,443	11/14/2001	Avi J. Ashkenazi	P2730P1C12	2356
35489	7590	03/19/2004	EXAMINER	
HELLER EHRMAN WHITE & MCAULIFFE LLP			KEMMERER, ELIZABETH	
275 MIDDLEFIELD ROAD			ART UNIT	
MENLO PARK, CO 94025-3506			PAPER NUMBER	
			1646	

DATE MAILED: 03/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/990,443	Applicant(s) ASHKENAZI ET AL.	
	Examiner Elizabeth C. Kemmerer, Ph.D.	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 August 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 119-124 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 119-124 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 14 November 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The preliminary amendments received 14 November 2001 and 03 September 2002 have been entered in full. Claims 1-118 are canceled. Claims 119-124 are under examination.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 24 May 2002 has been considered by the examiner. However, since the Blast results cited therein are not true publications with a publication date, they are not fully in compliance with 37 CFR 1.97 and thus they will not be printed on the face of the patent issuing from this application.

Specification

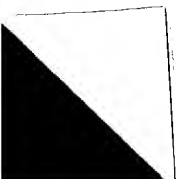
The specification should be reviewed for improper recitation of hyperlinks. All such recitations should be deleted or amended such that the hyperlinks are rendered inactive. See MPEP § 608.01.

35 U.S.C. §§ 101 and 112, First Paragraph

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:



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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 119-124 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility.

The claims are directed to antibodies that bind a polypeptide corresponding to SEQ ID NO: 194, referred to in the specification as PRO1009. The utility and enablement of the antibody depends upon whether or not the polypeptide it binds has utility and enablement. Based on this sequence similarity, the specification asserts that PRO1009 is a new long chain acyl-CoA synthetase enzyme. A search of SEQ ID NO: 194 against publicly available sequence databases reveals that SEQ ID NO: 194 has only weak sequence similarity to prior art long chain acyl-CoA synthetases, so it is not clear that PRO1009 is truly a new member of this protein family. Also, the prior art indicates that the members of this protein family have distinct tissue distribution and subcellular location, and are regulated independently during cellular differentiation and by diverse hormones and nuclear transcription factors. Based on these differences, each member of this protein family has distinct roles to play in lipid metabolism (see Coleman et al., 2002, J. Nutr. 132:2123-2126 for a review). The instant specification does not disclose any additional information regarding PRO1009 such as subcellular location, timing of regulation during cellular differentiation, which hormones or transcription factors regulate PRO1009, and what physiological significance PRO1009 has. Therefore, this asserted utility is not substantial, as significant further research

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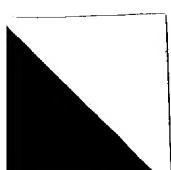
would be required by the skilled artisan to determine how to use the PRO1009 protein in a real-world, ready to use way.

The specification also generally asserts that all of the disclosed PRO polypeptides will be useful for a number of purposes; however, none of these asserted uses meet the three-pronged requirement of 35 U.S.C. § 101 regarding utility, namely, that the asserted utility be credible, specific and substantial. The asserted utilities will each be addressed in turn.

1) the PRO polypeptide can be used to isolate other polypeptides to which it binds: This asserted utility is not specific or substantial. Since the same can be done with any polypeptide, the asserted utility is not specific to the claimed PRO1009 polypeptides. Furthermore, since the specification does not disclose how PRO1009 or its binding partners can be used, significant further research would be required of the skilled artisan to determine how to use the claimed polypeptide or its binding partner. Since the asserted utility is not presented in a ready to use, real-world application, the asserted utility is not substantial.

2) the PRO polypeptide can be used as a molecular weight marker: This asserted utility is not specific. Since the same can be done with any polypeptide, the asserted utility is not specific to the claimed PRO1009 polypeptides.

3) the PRO polypeptide can be used in tissue typing: This asserted utility is not specific or substantial. With the exception of a few housekeeping genes, all polypeptides have a tissue specific pattern of expression, and thus virtually any



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polypeptide can be used in tissue typing. Thus, the asserted utility is not specific to PRO1009.

4) the PRO polypeptide can be used in therapy: This asserted utility is not specific or substantial. Since a defect in any polypeptide is likely to cause a disease of some sort, every polypeptide is a target for drug development. Thus, the asserted utility is not specific to the claimed PRO1009 polypeptide. Furthermore, the specification does not disclose a nexus between any specific disease states and a change in amount or form of PRO1009. Significant further research would have to be conducted to identify such a nexus. Therefore, the asserted utility is not substantial.

5) the PRO polypeptide can be used to identify agonists or antagonists: Since the same can be done with any polypeptide, the asserted utility is not specific to the claimed PRO1009 polypeptides. Furthermore, since no activity has been assigned to PRO1009, the assays cannot be conducted until the specific biological activities of PRO1009 are determined empirically. Therefore, the asserted utility is also not substantial.

The specification also discloses that PRO1009 tested positive in the gene amplification assay (Example 170, pp. 539-555). This information provides a credible, specific and substantial utility for PRO1009 nucleic acids, but not for PRO1009 polypeptides or antibodies. The preliminary data in the specification were not supported by analysis of mRNA or polypeptide expression, for example. Also, the literature reports that it does not necessarily follow that an increase in gene copy number results in increased gene expression and increased polypeptide expression, such that the

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claimed antibodies that bind the recited polypeptides would be useful for diagnosis of cancer or as a drug target. For example, Pennica et al. (1998, PNAS USA 95:14717-14722) disclose that:

"An analysis of *WISP*-1 gene amplification and expression in human colon tumors showed a correlation between DNA amplification and overexpression, whereas overexpression of *WISP*-3 RNA was seen in the absence of DNA amplification. In contrast, *WISP*-2 DNA was amplified in the colon tumors, but its mRNA expression was significantly reduced in the majority of tumors compared with the expression in normal colonic mucosa from the same patient."

See p. 14722, second paragraph of left column; pp. 14720-14721, "Amplification and Aberrant Expression of *WISPs* in Human Colon Tumors." See also Konopka (1986, PNAS USA 83:4049-4052), who state that

"Protein expression is not related to amplification of the *abl* gene but to variation in the level of *bcr-abl* mRNA produced from a single Ph1 template" (see abstract).

Finally, even if gene amplification correlates with increased transcription, it does not always follow that protein levels are also amplified. See Haynes et al. (1998, Electrophoresis 19:1862-1871), who studied more than 80 proteins relatively homogeneous in half-life and expression level, and found no strong correlation between polypeptide and transcript level. For some genes, equivalent mRNA levels translated into protein abundances which varied more than 50-fold. Haynes et al. concluded that the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript (p. 1863, second paragraph, and Figure 1). Therefore, the art indicates that it is not the norm that gene amplification, or even increased transcription, results in increased polypeptide levels.

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Therefore, the asserted utility is not substantial, as the real-world use has not been established. Thus, the proposed use of the claimed antibodies that bind PRO1009 polypeptides are simply starting points for further research and investigation into potential practical uses of the polypeptides. See *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), wherein the court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

Claims 119-124 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 119 and 124 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 119 recites an antibody that binds a polypeptide, whereas claim 124 recites an antibody that *specifically* binds the same polypeptide. Neither the art nor the specification provide a clear definition for, or distinction between, “binds” and “specifically binds”. Therefore, the metes and bounds of the claimed invention cannot be determined.

Priority

Applicant's claim for priority under 35 U.S.C. 120 and 119(e) is acknowledged. However, the applications upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 119-131 of this application. Specifically, since the instant specification fails to provide a disclosure meeting the requirements of 35 U.S.C. §§ 101 and 112, first paragraph, the claim for priority to any parent application is denied. The instant filing date, 14 November 2001, is thus used for the purposes of applying prior art.

35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 119 and 124 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 01/07628 A2 (published 01 February 2001).

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WO 01/07628 teaches an antibody that binds, or specifically binds, an isolated polypeptide having a sequence identical to SEQ ID NO: 194 as recited in the instant claims. See SEQ ID NO: 8 of WO 01/07628 and pp. 37-38. The antibodies disclosed by WO 01/07628 include monoclonal antibodies, humanized antibodies, antibody fragments and labeled antibodies (pp. 37-38).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D. whose telephone number is (571) 272-0874. The examiner can normally be reached on Monday through Thursday, 7:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne L. Eyler, Ph.D. can be reached on (571) 272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

ECK



ELIZABETH KEMMERER
PRIMARY EXAMINER